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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,563	07/07/2003	Gustavo C. Rodriguez	31168X	5832

7590 03/11/2004

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EXAMINER	
OSTRUP, CLINTON T	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/614,563	RODRIGUEZ, GUSTAVO C.	
	Examiner	Art Unit	
	Clinton Ostrup	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 34-43 are pending in this application.

Priority

Priority to Application Number 09/798,453, filed March 02, 2001, and 09/528,963, filed March 21, 2000 has been acknowledged.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 34-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 09/632,663 in view of claims 25-34 of US 2002/0061867 A1.

09/632,663 claims a composition comprising a progestin product, including levonorgestrel and derivatives of 17-alpha-hydroxy-progesterone or 19-nortestosterone; and a non-steroidal anti-inflammatory drug, such as the COX-2 selective inhibitors celecoxib and rofecoxib. However, the 09/632,663 does not specifically claim a composition comprising an estrogen or a Vitamin D product.

US 2002/0061867 A1 claims a composition comprising a vitamin D compound and a hormone product and claims the hormone product as comprising both estrogen and progestin.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the composition of 09/632,663 by adding estrogen and a vitamin D compound, as claimed by US 2002/0061867 A1, because of the reasonable expectation of obtaining a composition useful for the treatment of ovarian cancer with the desired added benefit of inhibiting the conversion of non-neoplastic ovarian epithelial cells to neoplastic cells.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 34-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Krasnow US 2003/0008870 A1.

Krasnow appears to be prior art under 35 U.S.C. 102(e) because it appears the instant claims are not supported by 09/528,963 because it lacks support for the

combined formulation comprising an estrogen a progestin product, and a non-steroidal anti-inflammatory drug, as claimed. Thus, it appears the instant claims have support and priority to 09/798,453, filed March 02, 2001 whereas Krasnow has a priority date of February 2, 2001.

Krasnow teaches compositions comprising celecoxib, ethinyl estradiol and levonorgestrel; compositions comprising rofecoxib, ethyl estradiol, and levonorgestrel; and compositions comprising celecoxib, ethinyl estradiol and derivatives of 17-alpha-hydroxy-progesterone or 19-nortestosterone, such as norethindrone acetate. Since ethyl estradiol is taught to be an estrogen in the instant specification (see: instant specification at page 3, line 9 – page 6, line 2), Krasnow meets the limitations of instant claims 34-38. See: page 17, [0160] –page 20, [0176]; page 23, [0206] – page 29, [0207]; page 30, claims 1-34; and abstract.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 34-36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chwalisz et al., 5,811,416 and further in view of Andrew S. Coco, M.D., Primary Dysmenorrhea. American Family Physician, August 1999, Volume 60, No. 2., pages 489-496 (Coco).

Chwalisz et al teaches as an aspect of the invention is to provide methods for the prevention and treatment of atherosclerotic vascular disease and hypertension in males and females with a combination of an endothelin antagonist and/or endothelin synthase inhibitor with steroid hormones (with an estrogen or with a combination of an estrogen and a progestin for females; with a progestin for males), and/or with an NO donor and/or NO substrate, and optionally with a cyclooxygenase inhibitor. Chwalisz et al teaches as another object of the invention is to provide hormone replacement therapy for peri- and post-menopausal females in need of such treatment with a combination of an endothelin antagonist and/or endothelin synthase inhibitor with steroid hormones (an estrogen or a combination of an estrogen and a progestin), and/or with a NO donor and/or NO substrate, and, optionally, with a cyclooxygenase inhibitor.

Chwalisz et al teaches estrogen and estrogen plus progestin combinations that are commercially available and teaches levonorgestrel and norethindrone acetate, as progestins that can be used in their invention. The reference teaches cyclooxygenase inhibitors include both COX-1 and COX-2 inhibitors, but describe that in particular, COX-2 inhibitors are preferred. See: col. 5, lines 34-50; col. 7, line 54 – col. 8, line 5; col. 9, line 15 – col. 10, line 61; col. 12, lines 30-41; claims 1 and 31-33; and abstract.

Although the reference suggests the combination of an estrogen, a progestin, and a COX inhibitor, specifically a COX-2 inhibitor, the reference lacks a specific example comprising the three components.

Coco teaches the treatment of primary dysmenorrhea using oral contraceptives and if the patient has a poor response to the oral contraceptive after three cycles to add NSAIDs to the treatment regimen. Moreover, Coco describes that "Because NSAIDs and oral contraceptives are so effective and work through different mechanisms, a combination of the two is a very attractive option in refractory cases." See: page 492, col. 1, second full paragraph – page 495, col. 1, end of first paragraph; and abstract.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have combined the specific components suggested by Chwalisz et al. into a single formulation because of a reasonable expectation of obtaining a composition for the treatment of hypertension while simultaneously providing the relief of pain associated with menstrual disorders, such as dysmenorrhea.

Claims 34-36 and 38-41 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chwalisz et al., 5,811,416 taken with Andrew S. Coco, M.D., Primary Dysmenorrhea. American Family Physician, August 1999, Volume 60, No. 2., pages 489-496 (Coco), as applied to claims 34-36 and 38 above, and further in view of Rodriguez et al., 6,034,074, which is available as prior art under 35 U.S.C. 102(a) and 102(e) because of its different inventive entity and its earlier publication date.

The combined references above teach a composition comprising an estrogen, a progestin, and a NSAID; however, the combined references lack the vitamin D compound as claimed in claims 39-41 and 43.

Rodriguez et al teach that vitamin D compounds prevent the development of ovarian cancer and that vitamin D compounds can be co-administered with estrogens and progestins to provide the dual benefit of contraceptive protection and prevention of ovarian cancer. See: col. 2, lines 15-36; col. 7, line 60 – col.8, line 25; col. 11, line 59 – col. 13, line 14.

It would have been obvious to one having ordinary skill in the art, at the time the invention was made to have modified the composition as taught by the combined references, Chwalisz et al and Coco, by adding vitamin D to the composition because of the reasonable expectation of obtaining a composition that could be used for the treatment of dysmenorrhea, while providing the added desired benefits of contraceptive protection and preventing ovarian cancers.

Claims 37 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chwalisz et al., 5,811,416 taken together with Andrew S. Coco, M.D., Primary Dysmenorrhea. American Family Physician, August 1999, Volume 60, No. 2., pages 489-496 (Coco), and Rodriguez et al., 6,034,074 and further in view of common knowledge in the art, as shown by the Physicians' Desk Reference, 54 Edition, 2000.

Celecoxib and refecoxib are both well-known COX-2 inhibiting, anti-inflammatory agents. Celecoxib is marketed under the tradename Celebrex® and refecoxib is marketed under the tradename Vioxx®. Both Celebrex® and Vioxx® have been shown

to exhibit anti-inflammatory, analgesic, and antipyretic activities and Vioxx® has eve been shown to provide analgesia for dysmenorrhea.

Therefore, it would have been obvious to on having ordinary skill in the art at the time the invention was made to have modified the compositions of the combined references above, by using well-known, readily available, easy to use COX-2 specific anti-inflammatory agents. One having ordinary skill in the art would have been motivated to combine celecoxib or refecoxib in the composition because of the reasonable expectation of obtaining a composition that provides contraceptive benefits, prevents ovarian cancer, and has an anti-inflammatory agent that has been demonstrated to have good analgesic properties, without the negative effects associated with dual inhibition of COX-1 and COX-2 inhibition.

Conclusion

If a copy of a provisional application listed on the bottom portion of the accompanying Notice of References Cited (PTO-892) form is not included with this Office action and the PTO-892 has been annotated to indicate that the copy was not readily available, it is because the copy could not be readily obtained when the Office action was mailed. Should applicant desire a copy of such a provisional application, applicant should promptly request the copy from the Office of Public Records (OPR) in accordance with 37 CFR 1.14(a)(1)(iv), paying the required fee under 37 CFR 1.19(b)(1). If a copy is ordered from OPR, the shortened statutory period for reply to this Office action will not be reset under MPEP § 710.06 unless applicant can demonstrate a substantial delay by the Office in fulfilling the order for the copy of the

provisional application. Where the applicant has been notified on the PTO-892 that a copy of the provisional application is not readily available, the provision of MPEP § 707.05(a) that a copy of the cited reference will be automatically furnished without charge does not apply.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clinton Ostrup whose telephone number is (571) 272-0582. The examiner can normally be reached on 8:00am - 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (571) 272-0584. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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